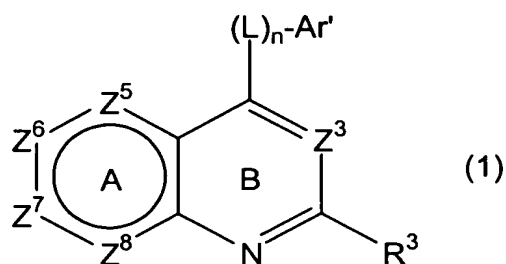


WHAT IS CLAIMED IS:

- 1 1. A method for counteracting a pathologic change in a signal-transduction
2 pathway involving a member of the steroid/thyroid hormone super-family, comprising
3 administering to a mammalian subject in need an effective amount of a compound capable of
4 inhibiting TGF- β signaling through a TGF- β receptor.
- 1 2. The method of claim 1 wherein the receptor is a steroid hormone receptor.
- 1 3. The method of claim 2 wherein the pathologic change is down- or up-
2 regulation of the steroid hormone receptor.
- 1 4. The method of claim 3 wherein the down- or up-regulation involves TGF- β .
- 1 5. The method of claim 3 wherein the down- or up-regulation is induced by
2 TGF- β .
- 1 6. The method of claim 1 wherein the pathologic change is a TGF- β induced
2 change in the activity or signaling of a steroid hormone receptor.
- 1 7. The method of claim 2 wherein the steroid hormone receptor is glucocorticoid
2 receptor.
- 1 8. The method of claim 1 wherein the receptor is a thyroid hormone receptor.
- 1 9. The method of claim 8 wherein the pathologic change is down- or up-
2 regulation of a thyroid hormone receptor.
- 1 10. The method of claim 9 wherein the down- or up-regulation involves TGF- β .
- 1 11. The method of claim 9 wherein the down- or up-regulation is induced by
2 TGF- β .

- 3 12. The method of claim 8 wherein the pathologic change is a TGF- β induced
4 change in the activity or signaling of a thyroid hormone receptor.
- 1 13. The method of claim 1 wherein the receptor is a retinoic acid receptor.
- 1 14. The method of claim 13 wherein the pathologic change is down- or up-
2 regulation of a retinoic acid receptor.
- 1 15. The method of claim 14 wherein the down- or up-regulation involves TGF- β .
- 1 16. The method of claim 14 wherein the down- or up-regulation is induced by
2 TGF- β .
- 1 17. The method of claim 13 wherein the pathologic change is a TGF- β induced
2 change in the activity or signaling of a retinoic acid receptor.
- 1 18. The method of claim 1 wherein the TGF- β receptor is a TGF β -R1 kinase.
- 1 19. The method of claim 18 wherein the compound is capable of binding to said
2 TGF β -R1 kinase.
- 1 20. The method of claim 19 wherein the compound is capable of binding to an
2 additional receptor kinase.
- 1 21. The method of claim 20 wherein the additional receptor kinase is an activin
2 receptor (Alk4).
- 1 22. The method of claim 1 wherein the compound is a non-peptide small
2 molecule.
- 1 23. The method of claim 22 wherein the compound is a small organic molecule.

1 24. The method of claim 23 wherein the small organic molecule is a compound of
2 formula (1)



3 or the pharmaceutically acceptable salts thereof
4 wherein R^3 is a noninterfering substituent;
5 each Z is CR^2 or N, wherein no more than two Z positions in ring A are N, and
6 wherein two adjacent Z positions in ring A cannot be N;
7 each R^2 is independently a noninterfering substituent;
8 L is a linker;
9 n is 0 or 1; and
10 Ar' is the residue of a cyclic aliphatic, cyclic heteroaliphatic, aromatic or
11 heteroaromatic moiety optionally substituted with 1-3 noninterfering substituents.

1 25. The method of claim 24 wherein the compound is a quinazoline derivative.

1 26. The method of claim 25 wherein Z^3 is N; and Z^5 - Z^8 are CR^2 .

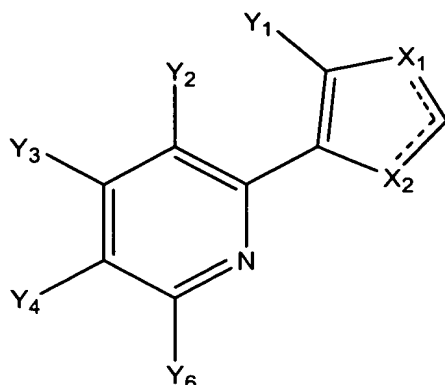
1 27. The method of claim 25 wherein Z^3 is N; and at least one of Z^5 - Z^8 is nitrogen.

1 28. The method of claim 25 wherein R^3 is an optionally substituted phenyl moiety.

1 29. The method of claim 28 wherein R^3 is selected from the group consisting of 2-
2 4-, 5-, 2,4- and 2,5-substituted phenyl moieties.

1 30. The method of claim 29 wherein at least one substituent of the phenyl moiety
2 is an alkyl(1-6C), or halo.

31. The method of claim 23, wherein the small organic molecule is a compound of formula (2)

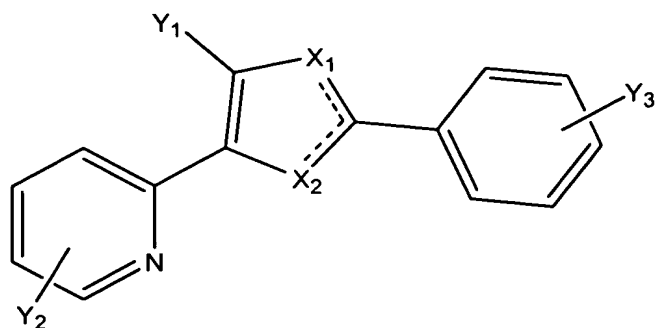


wherein Y₁ is phenyl or naphthyl optionally substituted with one or more substituents selected from halo, alkoxy(1-6 C), alkylthio(1-6 C), alkyl(1-6 C), haloalkyl (1-6 C), -O-(CH₂)_m-Ph, -S-(CH₂)_m-Ph, cyano, phenyl, and CO₂R, wherein R is hydrogen or alkyl(1-6 C), and m is 0-3; or phenyl fused with a 5- or 7-membered aromatic or non-aromatic ring wherein said ring contains up to three heteroatoms, independently selected from N, O, and

Y₂, Y₃, Y₄, and Y₅ independently represent hydrogen, alkyl(1-6C), alkoxy(1-6 C), haloalkyl(1-6 C), halo, NH₂, NH-alkyl(1-6C), or NH(CH₂)_n-Ph wherein n is 0-3; or an adjacent pair of Y₂, Y₃, Y₄, and Y₅ form a fused 6-membered aromatic ring optionally containing up to 2 nitrogen atoms, said ring being optionally substituted by one or more substituents independently selected from alkyl(1-6 C), alkoxy(a-6 C), haloalkyl(1-6 C), halo, NH₂, NH-alkyl(1-6 C), or NH(CH₂)_n-Ph, wherein n is 0-3, and the remainder of Y₂, Y₃, Y₄, and Y₅ represent hydrogen, alkyl(1-6 C), alkoxy(1-6C), haloalkyl(1-6 C), halo, NH₂, NH-alkyl(1-6 C), or NH(CH₂)_n-Ph wherein n is 0-3; and

one of X₁ and X₂ is N and the other is NR₆, wherein R₆ is hydrogen or alkyl(1-6 C).

32. The method of claim 23 wherein the small organic molecule is a compound of formula (3)



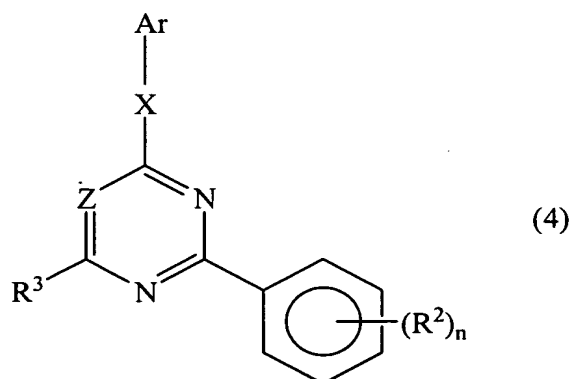
wherein Y_1 is naphthyl, anthracenyl, or phenyl optionally substituted with one or more substituents selected from the group consisting of halo, alkoxy(1-6 C), alkylthio(1-6 C), alkyl(1-6 C), -O-(CH₂)-Ph, -S-(CH₂)_n-Ph, cyano, phenyl, and CO₂R, wherein R is hydrogen or alkyl(1-6 C), and n is 0, 1, 2, or 3; or Y_1 represents phenyl fused with an aromatic or non-aromatic cyclic ring of 5-7 members wherein said cyclic ring optionally contains up to two heteroatoms, independently selected from N, O, and S;

Y_2 is H, NH(CH₂)_n-Ph or NH-alkyl(1-6 C), wherein n is 0, 1, 2, or 3;

Y_3 is CO₂H, CONH₂, CN, NO₂, alkylthio(1-6 C), -SO₂-alkyl(C1-6), alkoxy(C1-6), SONH₂, CONHOH, NH₂, CHO, CH₂NH₂, or CO₂R, wherein R is hydrogen or alkyl(1-6 C);

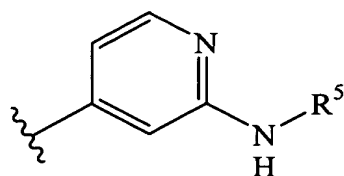
one of X_1 and X_2 is N or CR', and other is NR' or CHR' wherein R' is hydrogen, OH, alkyl(C-16), or cycloalkyl(C3-7); or when one of X_1 and X_2 is N or CR' then the other may be S or O.

33. The method of claim 23 wherein the small organic molecule is a compound of formula (4)



and the pharmaceutically acceptable salts and prodrug forms thereof; wherein

Ar represents an optionally substituted aromatic or optionally substituted heteroaromatic moiety containing 5-12 ring members wherein said heteroaromatic moiety contains one or more O, S, and/or N with a proviso that the optionally substituted Ar is not



wherein R⁵ is H, alkyl (1-6C), alkenyl (2-6C), alkynyl (2-6C), an aromatic or heteroaromatic moiety containing 5-11 ring members;

X is NR¹, O, or S;

R¹ is H, alkyl (1-8C), alkenyl (2-8C), or alkynyl (2-8C);

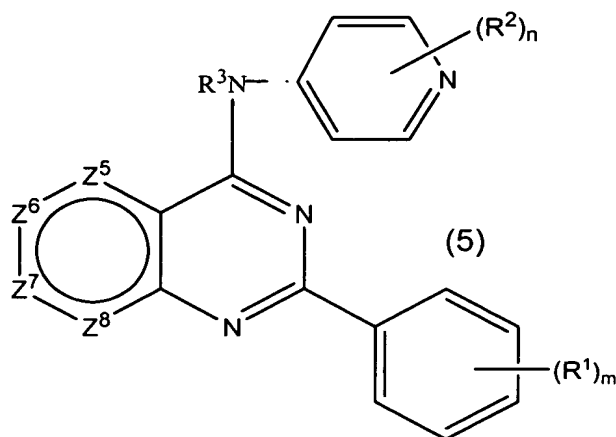
Z represents N or CR⁴;

each of R³ and R⁴ is independently H, or a non-interfering substituent;

each R² is independently a non-interfering substituent; and

n is 0, 1, 2, 3, 4, or 5. In one embodiment, if n>2, and the R²'s are adjacent, they can be joined together to form a 5 to 7 membered non-aromatic, heteroaromatic, or aromatic ring containing 1 to 3 heteroatoms where each heteroatom can independently be O, N, or S.

34. The method of claim 23 wherein the small organic molecule is a compound of formula (5)



or the pharmaceutically acceptable salts thereof;

wherein each of Z⁵, Z⁶, Z⁷ and Z⁸ is N or CH and wherein one or two Z⁵, Z⁶, Z⁷ and Z⁸ are N and wherein two adjacent Z positions cannot be N;

- 6 wherein m and n are each independently 0-3;
7 wherein two adjacent R¹ groups may be joined to form an aliphatic
8 heterocyclic ring of 5-6 members;
9 wherein R² is a noninterfering substituent; and
10 wherein R³ is H or CH₃.